Final report summary:

Are chickenpox and shingles risk factors for stroke?

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PRINCIPAL INVESTIGATOR: DR SARA THOMAS
INSTITUTION: LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE
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Why did we fund this research?

Little is known about how infections may increase a person’s risk of stroke. It has previously been suggested that strokes can be triggered by infections of an adult’s breathing system (respiratory infection) and urine drainage system (urinary tract infection). However, the role of infection in childhood stroke remains especially unclear.

An ‘infectious agent’ is anything that can enter the body and cause an infection, such as a virus or bacteria. One infectious agent identified as a possible trigger for stroke is the ‘varicella-zoster’ virus. It causes chickenpox following a first ‘primary infection’, and shingles after reactivation of a hidden ‘dormant infection’.

There are many case reports of stroke occurring in children soon after chickenpox, but chickenpox is very common in childhood, hence this may be due to chance. Two research studies have already suggested that children with stroke have a more frequent history of chickenpox compared to children without stroke or compared to the background child population. However, both studies were very small and again, did not take other risk factors for stroke into account.

Two reports from a study of Taiwanese adults have also shown that those who developed shingles were at 30% increased risk of stroke in the following year, and those with ophthalmic shingles (in the area around the eye) had more than four times the risk of stroke. However, these studies did not take into account all other risk factors for stroke.

The aim of this project was to better understand how the varicella zoster virus might increase the risk of stroke in adults and in children, and if so, whether vaccination reduces this risk. Rigorous, population-based studies were needed, with detailed assessment of the potentially protective effects of vaccination and antiviral medications used to treat varicella-zoster virus infections both in adults and in children.

What did the researchers do?

Two studies were conducted using patient information from the UK; a third study was conducted using patient information from the US.

The first study investigated whether children or adults who develop chickenpox are at an increased risk of stroke within the first 12 months of illness onset. The second study investigated whether adults who develop shingles are at an increased risk of stroke within the first 12 months. To answer the questions from both these studies, pre-collected anonymised data was used from very large UK general practice (GP) databases.

The third study investigated whether vaccinating older adults against shingles could reduce their risk of stroke after shingles. The shingles vaccine was only recently introduced to the UK in 2013, but it has been available in the US since 2006. Therefore, anonymised medical data from older individuals in the USA was used in this study.

All three studies investigated cases of first time stroke after chickenpox or shingles. They did not investigate cases of recurrent stroke.
What did the research find?

In the first study, a four-fold increased risk of stroke was found in 49 children (n=49) during the first six months after them developing chickenpox. The study found a smaller, less convincing increased risk of stroke in the first six months after chickenpox in adults (n=241). For both children and adults, there was little evidence of any increased risk of stroke in the 7-12 months after chickenpox.

Although the study provided new evidence that children who develop chickenpox are at an increased risk of stroke within the first six months, the baseline risk of stroke is extremely low in children. Therefore, even a four-fold increased risk after chickenpox still translates into only a very small stroke risk overall. Nevertheless, the results suggest that stroke is a rare complication of chickenpox in children. Better understanding of how stroke may be triggered by the varicella-zoster virus (which causes both chickenpox and shingles) could result in strategies to prevent childhood stroke in the future.

The second study was in adults who had a first ever episode of both shingles and stroke during follow-up. In the first four weeks after developing shingles, the stroke rate was one-and-a-half fold that of other time periods (n=6,584). This increased risk after shingles resolved gradually over a six-month period. Among patients who developed shingles around the eye, the stroke risk was higher, up to a three-fold increased risk in the five to 12 weeks after shingles onset.

About half the patients with shingles received oral antiviral treatment, and the risk of stroke after shingles was lower in these patients compared to those who were not treated with antivirals. This suggests that oral antiviral therapy given after shingles may help to reduce any post-shingles stroke risk. This suggests that the relatively low prescribing rates of antiviral therapy for shingles in UK general practice needs to be improved.

Using data from the US, the third study showed an almost two-and-a-half fold increased rate of stroke in the first week after shingles (and also over a one-and-a-half fold increased rate of heart attacks). As with the previous study, risk levels returned to normal within six months. The team found no evidence to suggest that patients who received the shingles vaccine were less susceptible to stroke after shingles. However, this finding requires further study due to the low vaccine uptake in the US study population.

The study investigating chickenpox and stroke was published in the journal Clinical and Infectious Diseases in October 2013.

The study investigating shingles and stroke was published in the journal Clinical and Infectious Diseases in April 2014.

The study investigating whether the risk of stroke after shingles might be modified by the shingles vaccine was published in the journal PLOS Medicine in 2015.

What does this mean for those with chickenpox or shingles?

Children who develop chickenpox may be at a four-fold increased risk of stroke for the following six months. However, stroke in children is still rare and the finding translates into a very small actual increase in their stroke risk.

The risk of stroke also appears to increase for adults during the six months after having shingles. This is particularly within the first few weeks, and for individuals with shingles around the eye. Oral antiviral drugs used to treat shingles may be able to reduce this risk. This suggests that the prescribing rate of these drugs in the UK needs to be improved.

The shingles vaccine was introduced to the UK in 2013. It might also reduce a temporarily increased risk of stroke in adults after shingles, but more research is necessary.
References


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